Non-Ablative Fractional Laser Provides Long-Term Improvement of Mature Burn Scars–A Randomized Controlled Trial With Histological Assessment

Elisabeth H. Taudorf, MD,[1*] Patricia L. Danielsen, MD, PhD,[1] Ida F. Paulsen, MD,[2] Katrine Togsverd-Bo, MD, PhD,[2] Christine Dierickx, MD,[3] Uwe Paasch, MD, PhD,[4] and Merete Haedersdal, MD, PhD, DMSc[1]

[1]*Department of Dermatology, Bispebjerg Hospital, University of Copenhagen, Denmark*

[2]*Clinic for Plastic Surgery, Burn Treatment and Breast Surgery, Copenhagen University Hospital, Rigshospitalet, Denmark*

[3]*Skin and Laser Center, Boom, Belgium*

[4]*Departments of Dermatology, Venereology and Allergology, University of Leipzig, Germany*

Background and Objectives: Non-ablative fractional laser-treatment is evolving for burn scars. The objective of this study was to evaluate clinical and histological long-term outcome of 1,540 nm fractional Erbium: Glass laser, targeting superficial, and deep components of mature burn scars.

Materials & Methods: Side-by-side scar-areas were randomized to untreated control or three monthly non-ablative fractional laser-treatments using superficial and extra-deep handpieces. Patient follow-up were at 1, 3, and 6 months. Primary outcome was improvement in overall scar-appearance on a modified-Patient-and-Observer-Scar-Assessment-Scale (mPOSAS, 1 = "normal skin", 10 = "worst imaginable scar"). Secondary outcomes included histology, patient satisfaction (0–10), patient-assessed improvement, and safety.

Results: Study was completed by 17 of 20 randomized patients with normotrophic ($n = 11$), hypertrophic ($n = 5$) or atrophic ($n = 1$) scars. Scar-appearance improved from laser-treatments ($P < 0.001$ vs. untreated) and histology at 6 months supported collagen-remodeling. Improvement appeared continuously during the post-operative period (mPOSAS baseline: 7 [5–8], 6 months: 4 [3–5] $P = < 0.001$). At 6 months, patients were satisfied with treatment (6 [3–9]) and 82% reported improved scar-texture. Treatments caused mild to moderate pain (4 [2–7]). Adverse effects decreased during follow-up and at final assessment, discrete erythema, hyperpigmentation or imprints from laser-grid were present in 11 patients. No patients experienced worsening of scar-appearance.

Conclusions: Combined superficial and deep non-ablative fractional laser-treatments induce long-term clinical and histological improvement of mature burn scars. Lasers Surg. Med.

Key words: burns; cosmetic surgery; laser treatment; non-ablative Erbium: glass laser; photothermolysis; skin grafts; scar texture

INTRODUCTION

Burn injuries affect people of all ages and cultures and cause severe morbidity and mortality. In the United States, 450,000 individuals received medical treatment and 3,400 died of burn injuries in 2012 [1]. Despite advances in initial care and surgical procedures [2], burns often heal with conspicuous scar patterns of varying relief, texture and dyspigmentation. In addition, scars may cause psychological discomfort, neuropathic pain, itching, and contractures [3]. The poor cosmetic outcome and function in these scars have traditionally been difficult to treat. Thus, new approaches to treatment are needed.

Fractional lasers are evolving treatment modalities for burn scars. Two types of fractional laser techniques are available; non-ablative fractional laser (NAFL) creates columns of coagulated tissue and leaves the skin barrier intact [4], while ablative fractional laser (AFL) disrupts the epidermis and vaporizes vertical channels into the skin [5,6]. Both techniques induce wound healing response

Abbreviations: NAFL, Non-ablative fractional laser; AFL, Ablative fractional laser; Mfu, months follow-up; mPOSAS, modified Patient and Observer Scar Assessment Scale; EHT, Elisabeth Hjardem Taudorf; MH, Merete Haedersdal; XD^{TM}, Extra Deep handpiece; XF^{TM}, Extra Fast handpiece; VAS, Visual Analog Scale; RCT, Randomized Controlled Trial

Conflict of Interest Disclosures: All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and have disclosed the following: [Laser equipment was provided to Merete Haedersdal by Palomar Medical Technologies, Burlington, MA, USA. Uwe Paasch received a grant to cover laboratory costs. The company did not have any role in design or conduct of the trial and had no access to study data or preparation of the manuscript.].

*Correspondence to: Elisabeth H. Taudorf, MD, Department of Dermatology D-92 Bispebjerg Hospital, University of Copenhagen Bispebjerg Bakke 23, DK-2400 Copenhagen NV, Denmark. E-mail: ehtaudorf@dadlnet.dk

Accepted 28 July 2014
Published online in Wiley Online Library (wileyonlinelibrary.com).
DOI 10.1002/lsm.22289

and collagen remodeling in healthy skin and thereby hold the potential to improve scar tissue [4,6,7].

A new "Laser Scar Treatment Algorithm" that recommends NAFL and AFL in the routine treatment of burn scars has been proposed in a recent expert consensus report [8]. Both non-ablative and ablative techniques have shown promising outcomes in treatment of mature burns scars; NAFL has been investigated in one blinded randomized controlled trial [9], in two uncontrolled open studies [10,11] and in a case report [12], while the evidence of AFL as monotherapy for burn scars includes two uncontrolled open studies [13,14] and four case reports [15–18]. So far, studies have evaluated treatment responses up to a maximum of 3 months after both NAFL and AFL and long-term treatment response remains to be evaluated. The histological burn scar response to fractional laser treatment has been investigated in two previous studies of AFL-treatment [13,14], while it is yet to be explored after NAFL-treatment.

Fractional lasers are able to target the delivered energy at different compartments of the skin [19]. It has been hypothesized that penetration depth of laser energy ideally has to be targeted at the entire thickness of scar tissue [8,9,11]. However, the effect of extending NAFL-treatment to deeper parts of burn scars remains to be clarified. Thus, the objective of this study was to evaluate clinical and histological long-term outcome of 1,540 nm NAFL-treatments targeting superficial and deep components of mature burn scars.

MATERIALS AND METHODS

Study Design

A randomized controlled trial with on-site blinded clinical evaluations and 1, 3, and 6 months follow-up (mfu). Study was approved prior to initiation by the Danish Research Ethics Committee (No.: H3-2009-149) and registered 12th of December 2013 at Clinicaltrials.gov (No.: NCT02014298). All study participants provided written informed consent.

Patients

Patients with scars from deep second or third degree burns were recruited from November 2011 to January 2012 at Clinic for Plastic Surgery, Burn Treatment and Breast Surgery, Copenhagen University Hospital, Rigshospitalet, Denmark. Inclusion, treatments and follow-up visits were performed from January to September 2012 at the Department of Dermatology, Bispebjerg Hospital, Denmark.

Eligible patients were adults aged 18–60 years with Fitzpatrick skin type I–III [20], burn scar duration of at least one year, a total scar area allowing selection of two similar side-by-side test areas, and no mental conditions associated with a risk of poor protocol outcome. Atrophic, normotrophic, and hypertrophic burn scars were accepted for inclusion regardless of previous skin-grafting. Exclusion criteria were pregnancy, lactation, tendency to form keloid, and use of certain systemic treatments within the last six months such as anticoagulants, oral retinoids, anti-inflammatory or immunosuppressive drugs. When included, study areas should appear without suntan, wounds or infection and any previous treatments with laser, intense pulsed light, dermabrasion, chemical peel or filler were not allowed.

Laser Treatments and Study Procedures

Two side-by-side square areas of minimum 1.5×3 cm with similar burn scar appearance received three NAFL-treatments at 4–6 weeks intervals and served as untreated control, respectively. Randomization was performed immediately before first laser treatment by patients receiving opaque, sealed envelopes that were mixed and consecutively numbered by an appointed nurse before study initiation.

All treatments were performed by the same physician (EHT) using a 1,540 nm Erbium: Glass NAFL (StarLux-500^{TM}, Palomar Medical Technologies, Inc., Burlington, MA, USA). A combined approach to target superficial and deep compartments of the skin was applied by utilizing tissue compression to avoid scattering of laser energy with an extra deep (XD^{TM}) handpiece, followed by a superficial extra fast (XF^{TM}) handpiece. The XD^{TM} handpiece delivered three stacked pulses in 10 passes without overlap between adjacent laser grids using energy settings of 70 mJ/microbeam and 15 ms pulse durations. Immediately afterwards, XF^{TM} handpiece delivered two passes of single pulses with 50% overlap between adjacent laser grids using energy settings of 50 mJ/microbeam and 15 ms pulse durations. Cold air-cooling was administered during treatments (CryoAir, MecoTec GmbH, Germany).

Biopsies were collected from scar tissue at baseline ($n = 17$) and 6 mfu ($n = 15$). At baseline, additional biopsies from normal skin were taken on an optional basis ($n = 13$). All biopsies were embedded in paraffin, stained with haematoxylin and eosin (H&E), cut vertically in 4–6 μm slices, and evaluated qualitatively with a calibrated bright field microscope (BX41, Olympus, Hamburg, Germany) equipped with calibrated CellF software (Olympus, Hamburg, Germany).

Clinical photos were taken under standardized lighting conditions and patient positioning with a digital camera (Canon EOS 1100D) using a 60 mm Macro objective and flash (Canon Macro Twin Lite MT-24EX).

Patient and Observer Scar Assessment Scale (POSAS)

Study outcomes were partially based on a validated Patient and Observer Scar Assessment Scale (POSAS) [21]. . POSAS ranges from 1–10, where one is comparable to "normal skin" and 10 represents "worst imaginable scar." The Observer-part of POSAS evaluates overall scar appearance, as well as specific assessments of vascularity, pigmentation, thickness, relief, pliability, and surface area [21,22]. In this study, registration of surface area was excluded since the test areas constituted a fixed size according to study procedures and thus, the scale is

subsequently referred to as modified POSAS (mPOSAS). In accordance with recent validation of POSAS for burn scars [23], the Patient-part of mPOSAS was omitted from data analyses, since it was difficult for the patients to apply.

Evaluation Criteria

Clinical evaluations were performed at baseline 1, 3, and 6 mfu. Primary outcome was evaluation of overall scar-appearance on mPOSAS by a blinded physician (MH). Based on mPOSAS reduction, we classified the improvement of treated area as mild (=1-point reduction), moderate (=2-point reduction) or significant (≥3-point reduction).

Secondary outcomes were patient satisfaction (0–10 categorical scale), patient-evaluated efficacy (1–5), qualitative histological evaluations of scar structure at 6 mfu, and safety. Safety parameters included pain during treatment (0–10), immediate occurrence of edema, erythema, purpura, and blistering (0–3), 24-hour adverse effects (patient questionnaire) and adverse effects after 6 months, such as hyperpigmentation, erythema, imprints from laser grid and scarring (binary scale).

Statistical Analyses

Descriptive statistics were presented as medians and interquartile ranges (IQ ranges) since data did not follow Gaussian distributions tested by Shapiro–Wilk normality test. Friedman test was used for the comparison of more than two matched groups and Wilcoxon matched pairs test for two paired groups. A sample size of 16 patients provided 80% power to detect a difference of two on the 1–10 point mPOSAS with an estimated standard deviation of two and a two-tailed significance level of 5%. A total of 20 patients were included in order to consider the potential risk of drop-outs. Statistical analyses and graphical illustrations were performed with GraphPad Prism 5 (GraphPad Software, La Jolla, CA, USA). P-values < 0.05 were considered significant.

RESULTS

Twenty patients were randomized to treatment. Study population consisted of 11 females and 9 males of median 38 (24–46) years with Fitzpatrick skin types II ($n = 13$) and III ($n = 7$). Patients suffered from burn scars on trunk ($n = 6$) or extremities ($n = 14$), caused by fire ($n = 15$) or scalding ($n = 5$). Burn scars had lasted for a median of 6.5 (4–20) years and were stable at time of inclusion (Table 1). Three patients were excluded due to pregnancy ($n = 1$) and for personal reasons unrelated to study procedures ($n = 2$) (Fig. 1). All statistics are subsequently based on the 17 patients, who completed study.

TABLE 1. Baseline Demography and Burn Scar Characteristics

Baseline demography of included patients ($n = 20$)	
Age	38 (24–46)
Sex	
Women	$n = 11$ (55%)
Men	$n = 9$ (45%)
Skin type	
II	$n = 13$ (65%)
III	$n = 7$ (35%)
Burn scar characteristics	
Scar age (years)	7 (4–20)
Etiology of burn scar	
Fire	$n = 15$ (75%)
Scalding	$n = 5$ (25%)
Previous meshed skin grafting	
Yes	$n = 14$ (70%)
No	$n = 6$ (30%)
Scar location	
Thigh	$n = 5$ (25%)
Upper arm	$n = 5$ (25%)
Chest	$n = 4$ (20%)
Lower arm	$n = 2$ (10%)
Dorsum of hand	$n = 2$ (10%)
Back	$n = 2$ (10%)

Data are medians (IQ ranges) or numbers (%).

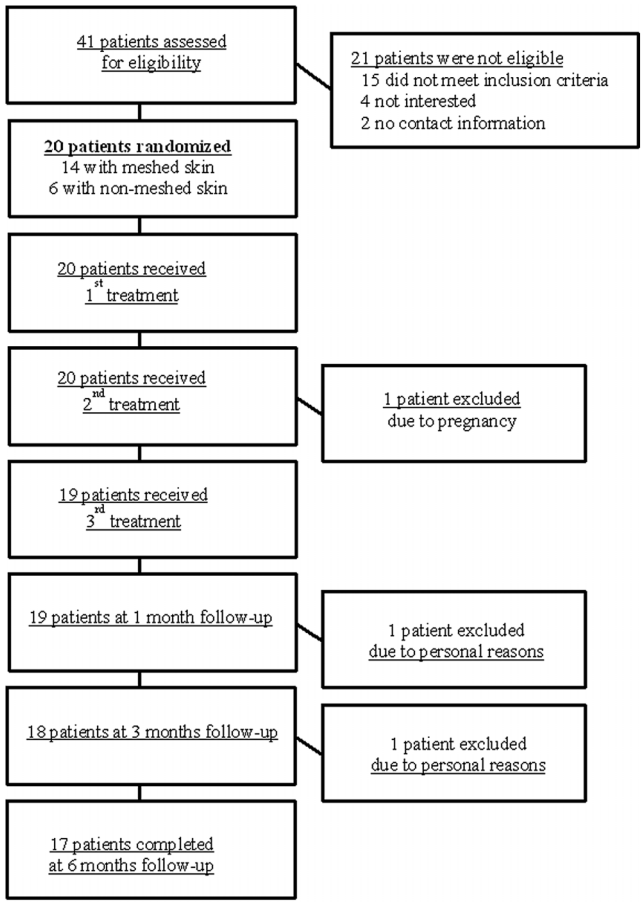

Fig. 1. Participant flow-chart.

Scar Characteristics

Scars were classified as normotrophic ($n = 11$), hypertrophic ($n = 5$) or atrophic ($n = 1$), and 12 of 17 scars had meshed skin-grafts. Clinically, grafted scars had characteristic patterns of varying thickness, texture and dyspigmentation (Fig. 2). All scars had loss of skin appendages such as hair follicles and glands and presented within the range of thin shiny surfaces to thick bulky lesions.

Improvement of Overall Scar-Appearance

At baseline, individual side-by-side test areas presented with similar overall scar-appearance of moderate to severe scarring (mPOSAS: 7 [5– 8], $P = 1$, Table 2, Fig. 2). NAFL-treated scars gradually improved throughout study period (1 mfu: 6 [5–7], 3 mfu: 5 [4–6], and 6 mfu: 4 [3–5], $P < 0.001$), while the control area remained stable ($P = 0.166$) (Table 2). Likewise, the treated area improved significantly in comparison to untreated control from baseline to 3 months ($P = 0.036$) as well as from 3 to 6 months ($P = 0.009$) (Table 2).

At 6 months the laser-treated scar area appeared smoother than untreated control in 15 of 17 patients (88%), particularly due to improved skin thickness ($P < 0.001$), relief ($P < 0.001$), and pliability ($P = 0.008$) (Table 2). Improvement was mild in two patients, moderate in seven patients and considerable in six patients. Normotrophic meshed skin-grafts were seen in five of the six patients with considerable improvement, and clinically, meshed-skin grafts tended to respond better to treatment than non-meshed skin ($P = 0.110$, Fig. 2).

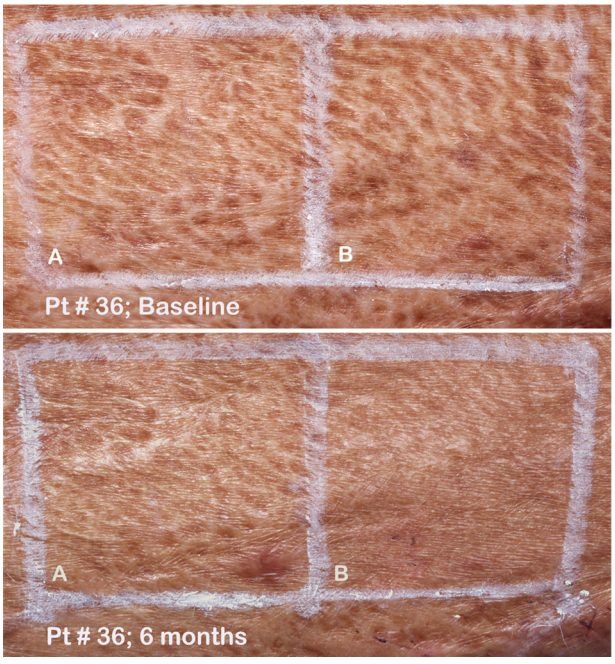

Fig. 2. Burn scar: Clinical improvement from baseline (top picture) to six months follow-up (lower picture)in agood-responding patientwith meshed skin-graft (treated in right area). Improvement on mPOSAS: 4 points.

TABLE 2. Clinical Burn Scar Appearance at Baseline and 1, 3, and 6 Months Follow-up

	Control area	Treated area	*P*
Overall impression			
Control and Treated area:			
Baseline	7 (5–8)	7 (5–8)	1.000
1 month	7 (5–8)	6 (5–7)	0.281
3 months	7 (5–8)	5 (4–6)	0.036
6 months	7 (5–7)	4 (3–5)	<0.001
P	0.166	<0.001	
Change:			
Baseline–3 months	0 (0–1)	1 (1–3)	0.036
3–6 months	0 (0–0)	1 (-1–2)	0.009
Baseline–6 months	0 (0–1)	2 (2–3)	<0.001
Thickness			
Change:			
Baseline–3 months	0 (0–0)	1 (1–2)	<0.001
3–6 months	0 (0–0)	0 (0–1)	0.233
Baseline–6 months	0 (0–0)	1 (1–2)	<0.001
Relief			
Change:			
Baseline–3 months	0 (0–0)	3 (2–4)	<0.001
3–6 months	0 (0–0)	0 (0–1)	0.821
Baseline–6 months	0 (0–0)	3 (2–4)	<0.001
Pliability			
Change:			
Baseline–3 months	0 (0–0)	1 (0–2)	0.034
3–6 months	0 (0–0)	0 (0–1)	0.071
Baseline–6 months	0 (0–0)	1 (0–2)	0.008
Vascularity			
Change:			
Baseline–3 months	0 (0–0)	-1 (-2–0)	0.002
3–6 months	0 (0–0)	1 (0–2)	0.004
Baseline–6 months	0 (0–1)	0 (-1–1)	0.092
Pigmentation			
Change:			
Baseline–3 months	0 (0–1)	1 (0–3)	0.397
3–6 months	0 (0–0)	0 (-1–1)	0.468
Baseline–6 months	0 (0–1)	1 (0–3)	0.208

Data are medians (IQ-ranges) based on clinical evaluations of the Observer-part from a modified Patient and Observer Scar Assessment Scale (mPOSAS).

Hypertrophic bulky scars achieved only mild to moderate improvement irrespectively of skin-grafting.

Patient Evaluations

In accordance with blinded physician's assessments, 14 of 17 patients (82%) reported visual improvement of scar texture at 6 mfu. Patient satisfaction was stable throughout the postoperative period with a median score of 6 (3–9) at final follow-up visit 6 months after treatment.

Histological Collagen Remodeling

Fifteen biopsies were qualitatively evaluated at baseline and 6 months post-treatment and compared to normal skin

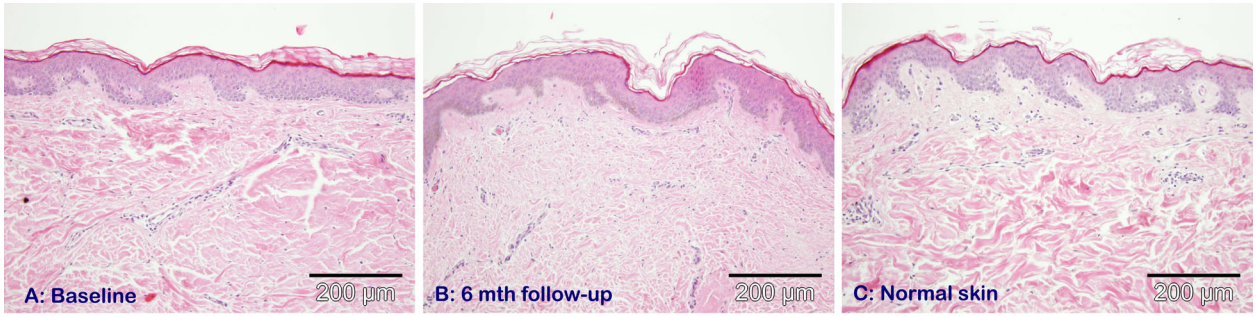

Fig. 3. Burn scar: Histology from a scar with meshed skin-graft (H&E stained). At baseline (pre-treatment) dermis presents with focal scar tissue, surface-paralleled thickened and centrally hyalinized collagen bundles and inflammation (left picture). At 6 months follow-up (post 3 non-ablative fractional laser treatments) the skin appears normal with uniform dense interwoven collagen fibers, re-established rete ridges at the dermal-epidermal junction, sparse inflammation and higher vascularization (middle picture). Normal skin from the same anatomical region is shown for comparison (right picture).

structure. The epidermal compartment presented with more prominent rete ridges in comparison to the flattened dermal-epidermal junction present in untreated baseline scar. In the dermal compartment, collagen structure changed from thick surface-paralleled hyalinised bundles to uniform dense interwoven fibers with higher vascularization. Overall, scar architecture was modified towards normal skin structure. Furthermore, inflammation decreased and was predominately found in the deep dermis after NAFL treatments (Fig. 3).

Safety

Patients experienced mild to moderate pain from treatments and pain intensity was similar during the three treatment sessions (VAS: 4 [2–7], $P = 0.374$). Immediate treatment reactions consisted of edema (85–95% of patients), erythema (90–100%), and purpura (50–80%), whereas no patients developed blisters (Table 3).

At 24 hours after treatment, patients reported redness (95–100% of patients), dryness (53–60%), swelling (26–40%), temperature sensibility (15–20%), flaking(15–16%), and blistering (0–5%) (Table 3). Post-operative skin reactions did not influence the patients' daily activities.

Majority of adverse effects were transient and overall decreased during the post-operative period. At final follow-up visit 6 months after treatment, 11 of 17 patients experienced discrete erythema ($n = 8$), hyperpigmentation ($n = 6$) or imprints from laser-grid ($n = 3$, Fig. 4) (Table 3). No patients had worsening of scar-appearance after NAFL.

TABLE 3. Treatment Responses and Adverse Effects After non-ablative Fractional Laser

Event	1st Treatment ($n = 20$)	2nd Treatment ($n = 20$)	3rd Treatment ($n = 19$)
Immediate response			
Edema	$n = 17$ (85%)	$n = 19$ ((95%)	$n = 18$ (95%)
Erythema	$n = 20$ (100%)	$n = 18$ (90%)	$n = 18$ (95%)
Purpura	$n = 16$ (80%)	$n = 10$ (50%)	$n = 12$ (63%)
Blistering	$n = 0$ (0%)	$n = 0$ (0%)	$n = 0$ (0%)
Other	$n = 0$ (0%)	$n = 0$ (0%)	$n = 0$ (0%)
24 hour response			
Swelling	$n = 8$ (40%)	$n = 8$ (40%)	$n = 5$ (26%)
Redness	$n = 19$ (95%)	$n = 20$ (100%)	$n = 19$ (100%)
Blistering	$n = 0$ (0%)	$n = 0$ (0%)	$n = 1$ (5%)
Flaking	$n = 3$ (15%)	$n = 3$ (15%)	$n = 3$ (16%)
Dryness	$n = 11$ (55%)	$n = 12$ (60%)	$n = 10$ (53%)
Oozing	$n = 0$ (0%)	$n = 0$ (0%)	$n = 1$ (5%)
Temperature sensibility	$n = 4$ (20%)	$n = 3$ (15%)	$n = 4$ (21%)
6 months follow-up ($n = 17$)			
Erythema			$n = 8$ (47%)
Hyperpigmentation			$n = 6$ (35%)
Visible grid pattern			$n = 3$ (18%)
Scarring			$n = 0$ (0%)

Data are number of patients (%).

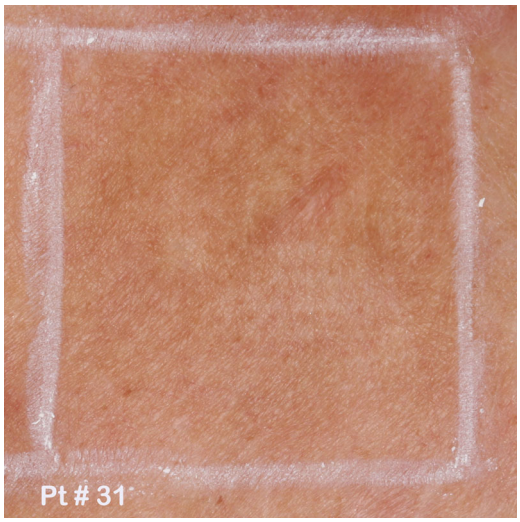

Fig. 4. Burn scar: Example of visible imprint from laser grid pattern in treated area at 6 months follow-up.

DISCUSSION

In this study, NAFL-treatment induced long-term improvement of mature burn scars. Clinical improvement was supported by histological collagen remodeling towards normal skin structure. Smoothening of scar texture appeared gradually and continued up to final follow-up at 6 months. Clinically, we found a tendency towards superior efficacy of NAFL-treatment in scars with normotrophic meshed skin-grafts. This observation might be explained by an increased remodeling potential of healthy skin-transplants compared to burned scar tissue.

Hypertrophic difficult-to-treat scars responded less favorably than normotrophic and atrophic scars in spite of the combined NAFL approach targeting superficial as well as deep scar components. A previous randomized controlled trial (RCT) investigated 1,540 nm superficially targeted NAFL for mature burn scars [9] and found a similar lack of improvement in thick bulky scars. Possibly, a better treatment response could have been achieved by additional treatment sessions or adjusted laser settings according to scar type. The penetration depth of NAFL has previously been reported up to approximately 2.2 mm [24] using compression technique. Whether hypertrophic burn scars may benefit from even deeper penetrating laser energy or by treatment with a combination of different laser types as suggested in one previous uncontrolled study [25], remains to be clarified in future RCTs.

In general, positive outcomes have been reported from NAFL [9–12] and AFL [13–18,25,26] for burn scars of mixed atrophic, normotrophic and hypertrophic appearances. These treatment modalities possess different advantages and disadvantages. Thus, NAFL-treatment is considered relatively safe due to intact epidermal barrier, which requires little or no topical anesthetics and causes minor post-treatment pain [9,11], minimal wound care, low risk of infections and no patient down-time. However, stamping with the NAFL handpieces is time-consuming, which hampers the treatment of large scar areas. Disruption of the skin barrier by AFL-treatment may increase the penetration depth up to 4.0 mm [8] and potentially increases the risk of post-treatment pain, infections and ulcers [14]. Typically, patient-recovery after AFL requires substantial wound care and lasts approximately one week [13,26]. The ablated channels generated by AFL may also serve as an alternative route for drug delivery. Thus, burn scars have previously been treated efficaciously with combinations of AFL and corticosteroids [26].

AFL-treatment has been shown histologically to induce collagen remodeling and molecular changes towards a normalized expression of type I and III collagen [13,14]. The present study adds information that histological collagen remodeling towards normal skin structure also takes place after NAFL-treatment.

Previously reported fractional laser treatment regimes for burn scars include various combinations of laser settings and up to seven treatment sessions at 1–3 month intervals [9–18,25,26]. The laser settings selected in this study were based on pilot studies (not shown) since no golden standard exists for NAFL-treatment of burn scars. Even though 15 of 17 patients had overall improvement of scar-appearance, 11 patients experienced one or more prolonged adverse effects such as erythema, hyperpigmentation or visible imprints from laser grid (Fig. 4). Overall, adverse effects were transient and decreased during post-operative follow-up towards a discrete appearance at study completion. Thus, 82% of patients reported improvement of scar appearance despite mild adverse effects. Still, the complication rates are somewhat higher than elsewhere reported [27,28], which may be explained by the application of multiple passes or high pulse energies. Moreover, visible imprints from laser grids have, to our knowledge, not previously been described.

These findings emphasize the need for individually adjusted laser settings that can be achieved by guidance from immediate biological skin responses to test treatments. Thus, NAFL-treatments should induce initial erythema without epidermal affection followed by oedema within a few minutes.

Based on the occurrence of adverse events we concluded that maximum tolerable settings had been applied without potential additional effect from increasing laser energy. However, decreased number of passes, individually adjusted laser settings or augmented intervals between treatments could possibly have improved the safety profile [8].

Study limitations included occasional incomplete blinding of evaluating physician due to prolonged erythema in treated area and small sample size. Size and distribution of patient population did not provide the power to make clear conclusions on the observed tendency towards superior efficacy of NAFL in normotrophic scars with meshed skin-grafts. Thus, future RCTs are needed to verify this trend.

In conclusions, this study shows that three 1,540 nm NAFL-treatments targeting superficial and deep

components of scar tissue lead to continuous and long-term clinical improvement of mature burn scars supported by histological collagen remodeling towards normal skin structure.

ACKNOWLEDGMENTS

The authors wish to thank our skilled study nurse Kirsten Svejstrup Thorn for taking care of the study patients and professional photographer Nis Kentorp for helping with clinical photos and illustrations.

REFERENCES

1. American Burn Association. at <www.ameriburn.org/resouces_factsheet.php>.
2. Orgill DP, Ogawa R. Current methods of burn reconstruction. Plast Reconstr Surg 2013;131:827e–836e.
3. Esselman PC, Thombs BD, Magyar-Russell G, Fauerbach JA. Burn rehabilitation: State of the science. Am J Phys Med Rehabil 2006;85:383–413.
4. Manstein D, Herron GS, Sink RK, Tanner H, Anderson RR. Fractional photothermolysis: A new concept for cutaneous remodeling using microscopic patterns of thermal injury. Lasers Surg Med 2004;34:426–438.
5. Hantash BM, Bedi VP, Chan KF, Zachary CB. Ex vivo histological characterization of a novel ablative fractional resurfacing device. Lasers Surg Med 2007;39:87–95.
6. Hantash BM, Bedi VP, Kapadia B, Rahman Z, Jiang K, Tanner H, Chan KF, Zachary CB. In vivo histological evaluation of a novel ablative fractional resurfacing device. Lasers Surg Med 2007;39:96–107.
7. Laubach H-J, Tannous Z, Anderson RR, Manstein D. Skin responses to fractional photothermolysis. Lasers Surg Med 2006;38:142–149.
8. Anderson RR, Donelan MB, Hivnor C, Greeson E, Ross EV, Shumaker PR, Uebelhoer NS, Waibel JS. Laser treatment of traumatic scars with an emphasis on ablative fractional laser resurfacing: Consensus report. JAMA Dermatol 2013; 1–7. doi: 10.1001/jamadermatol.2013.7761
9. Haedersdal M, Moreau KER, Beyer DM, Nymann P, Alsbjørn B. Fractional nonablative 1540 nm laser resurfacing for thermal burn scars: A randomized controlled trial. Lasers Surg Med 2009;41:189–195.
10. Vasily D, Cerino M, Ziselman E, Tannous ZS. Non-ablative fractional resurfacing of surgical and post-traumatic scars. J drugs dermatol 2009;8:998–1005.
11. Waibel J, Wulkan AJ, Lupo M, Beer K, Anderson RR. Treatment of burn scars with the 1,550 nm nonablative fractional erbium laser. Lasers Surg Med 2012;44:441–446.
12. Waibel J, Beer K. Fractional laser resurfacing for thermal burns. J Drugs Dermatol 2008;7:59–61.
13. Qu L, Liu A, Zhou L, He C, Grossman PH, Moy RL, Mi QS, Ozog D. Clinical and molecular effects on mature burn scars after treatment with a fractional CO(2) laser. Lasers Surg Med 2012;44:517–524.
14. Ozog DM, Liu A, Chaffins ML, Ormsby AH, Fincher EF, Chipps LK, Mi QS, Grossman PH, Pui JC, Moy RL. Evaluation of clinical results, histological architecture, and collagen expression following treatment of mature burn scars with a fractional carbon dioxide laser. JAMA dermatol 2013;149:50–57.
15. Bowen R. A novel approach to ablative fractional treatment of mature burn scars. J drugs dermatol 2010;9:389–392.
16. Haedersdal M. Fractional ablative CO2 laser resurfacing improves a thermal burn scar. JEADV 2009;23:1340–1341.
17. Cho S, Lee S, Chung W, Kang J, Kim Y. Treatment of burn scar using a carbon dioxide fractional laser. J Drugs Dermatol 2010;9:173–175.
18. Waibel JS, Beer K. Ablative fractional laser resurfacing for the treatment of a third-degree burn. J Drugs Dermatol 2009;8:294–297.
19. Taudorf EH, Haak CS, Erlendsson AM, Philipsen PA, Anderson RR, Paasch U, Haedersdal M. Fractional ablative erbium YAG laser: Histological characterization of relationships between laser settings and micropore dimensions. Lasers Surg Med 2014; 1–9. doi: 10.1002/lsm.22228
20. Fitzpatrick T. The validity and practicality of sun-reactive skin types I through VI. Arch Dermatol 1988;124:869–871.
21. Van de Kar AL, Corion LUM, Smeulders MJC, Draaijers LJ, van der Horst CMAM, van Zuijlen PPM. Reliable and Feasible Evaluation of Linear Scars by the Patient and Observer Scar Assessment Scale. Plast Reconstr Surg 2005;116:514–522.
22. Tyack Z, Wasiak J, Spinks A, Kimble R, Simons M. A guide to choosing a burn scar rating scale for clinical or research use. Burns 2013; 1–10. doi: 10.1016/j.burns.2013.04.021
23. Van der Wal MBA, Tuinebreijer WE, Bloemen MCT, Verhaegen PDHM, Middelkoop E, van Zuijlen PPM. Rasch analysis of the Patient and Observer Scar Assessment Scale (POSAS) in burn scars. Qual Life Res 2012;21:13–23.
24. Zelickson B, Walgrave S, Al-Arashi M, Yaroslavsky I, Altshuler G, Childs J, Smirnov M, Tabatadze D. Evaluation of a fractional laser with optical compression pins. Lasers Surg Med 2011;43:137–142.
25. Hultman CS, Edkins RE, Wu C, Calvert CT, Cairns Ba. Prospective, before-after cohort study to assess the efficacy of laser therapy on hypertrophic burn scars. Ann Plast Surg 2013;70:521–526.
26. Waibel JS, Wulkan AJ, Shumaker PR. Treatment of hypertrophic scars using laser and laser assisted corticosteroid delivery. Lasers Surg Med 2013;45:135–140.
27. Clayton JL, Edkins R, Cairns BA, Hultman CS. Incidence and management of adverse events after the use of laser therapies for the treatment of hypertrophic burn scars. Ann Plast Surg 2013;70:500–505.
28. Metelitsa AI, Alster TS. Fractionated laser skin resurfacing treatment complications: A review. Dermatol Surg 2010; 36:299–306.